

What is claimed is:

1. An isolated nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2.

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2. The isolated nucleic acid molecule of claim 1 that comprises the nucleotide sequence of SEQ ID NO:1.

10 3. A nucleic acid molecule that is a complement to said isolated nucleic acid molecule of claim 1.

4. A nucleotide sequence that hybridizes under stringent conditions to said complement of claim 3, provided that said nucleotide sequence does not encode human, murine or rat receptor activator of NF-κB ligand polypeptide.

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5. The isolated nucleic acid molecule of claim 1 that is DNA or RNA.

20 6. An isolated canine receptor activator of NF-κB ligand comprising the amino acid sequence of SEQ ID NO:2, or a fragment thereof, wherein said fragment binds to a canine receptor activator of NF-κB.

7. The isolated canine receptor activator of NF-κB ligand of claim 6, wherein said fragment is selected from the group consisting of:

from about residue 10 to about residue 275 of SEQ ID NO:2;

from about residue 30 to about residue 275 of SEQ ID NO:2;

from about residue 50 to about residue 275 of SEQ ID NO:2;

from about residue 150 to about residue 275 of SEQ ID NO:2;

from about residue 250 to about residue 275 of SEQ ID NO:2;

from about residue 255 to about residue 275 of SEQ ID NO:2;

from about residue 235 to about residue 255 of SEQ ID NO:2;

from about residue 215 to about residue 235 of SEQ ID NO:2;

from about residue 195 to about residue 215 of SEQ ID NO:2;

from about residue 175 to about residue 195 of SEQ ID NO:2
from about residue 155 to about residue 175 of SEQ ID NO:2;
from about residue 135 to about residue 155 of SEQ ID NO:2;
from about residue 95 to about residue 135 of SEQ ID NO:2;
from about residue 75 to about residue 95 of SEQ ID NO:2;
from about residue 55 to about residue 75 of SEQ ID NO:2;
from about residue 35 to about residue 55 of SEQ ID NO:2;
from about residue 15 to about residue 35 of SEQ ID NO:2;
from about residue 1 to about residue 15 of SEQ ID NO:2;
from about residue 125 to about residue 160 of SEQ ID NO:2;
from about residue 119 to about residue 153 of SEQ ID NO:2;
from about residue 175 to about residue 200 of SEQ ID NO:2;
from about residue 183 to about residue 192 of SEQ ID NO:2;
from about residue 200 to about residue 225 of SEQ ID NO:2;
from about residue 204 to about residue 211 of SEQ ID NO:2;
from about residue 195 to about residue 215 of SEQ ID NO:2;
from about residue 221 to about residue 227 of SEQ ID NO:2;
from about residue 110 to about residue 140 of SEQ ID NO:2; and
any combination thereof.

8. An immunogenic composition that comprises the canine receptor activator of NF- κ B ligand of claim 6.

5 9. The immunogenic composition of claim 8, that further comprises one or more additional elements selected from the group consisting of:

- (a) a foreign T helper lymphocyte epitope,
- (b) an element that targets the canine receptor activator of NF- κ B ligand immunogenic composition to an antigen presenting cell or a B-lymphocyte,

10 (c) an element that stimulates the immune system, and
(d) an element that optimizes presentation of the canine receptor activator of NF- κ B ligand to the immune system.

10. The immunogenic composition of claim 9, wherein the canine receptor activator of NF- κ B ligand is part of a fusion polypeptide.

11. The immunogenic composition of claim 9 that further comprises a duplication of at 5 least one element selected from the group consisting of a receptor activator of NF- κ B ligand B-cell epitope, a hapten and a combination thereof.

12. The immunogenic composition of claim 9, wherein said T-cell epitope is immunodominant in a mammal to be treated.

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13. The immunogenic composition of claim 9, wherein said foreign T-cell epitope is selected from the group consisting of a natural promiscuous T-cell epitope and an artificial MHC-II binding peptide sequence.

15 14. The immunogenic composition of claim 13, wherein said natural promiscuous T-cell epitope is selected from the group consisting of a Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagglutinin epitope, and a *P. falciparum* CS epitope.

20 15. The immunogenic composition of claim 14, wherein said Tetanus toxoid epitope is a Tetanus toxoid P2 epitope or a Tetanus toxoid P30 epitope.

25 16. The immunogenic composition of claim 9 (b), wherein said targeting element is selected from the group consisting of a substantially specific binding partner for a B-lymphocyte specific surface antigen, an APC specific surface antigen for which there is a receptor on the B-lymphocyte and the APC, and a combination thereof.

30 17. The immunogenic composition of claim 9(c), wherein said immune system stimulating element is selected from the group consisting of a cytokine, a hormone, and a heat-shock protein.

18. The immunogenic composition of claim 17, wherein the cytokine is selected from the group consisting of interferon *gamma*, Flt3L, interleukin 1, interleukin 2, interleukin

4, interleukin 6, interleukin 12, interleukin 13, interleukin 15, granulocyte-macrophage colony stimulating factor, and an effective fragment thereof: and wherein, the heat-shock protein is selected from the group consisting of HSP70, HSP90, HSC70, GRP94, calreticulin, and an effective fragment thereof.

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19. The immunogenic composition of claim 9 (d), wherein said immune system presenting element is a lipid selected from the group consisting of a palmitoyl group, a myristyl group, a farnesyl group, a geranyl-geranyl group, a GPI-anchor, and an N-acyl diglyceride group.

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20. The immunogenic composition of claim 9 that comprises

(i) at least two copies of the receptor activator of NF- κ B ligand polypeptide or the fragment thereof, or
(ii) a modified receptor activator of NF- κ B ligand polypeptide or a modified fragment thereof, wherein the modified receptor activator of NF- κ B ligand polypeptide or modified fragment thereof is linked to a carrier molecule.

15 21. A vaccine composition comprising an effective amount of the receptor activator of NF- κ B ligand immunogenic composition of claim 6, and a pharmaceutically acceptable carrier.

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22. The vaccine composition of claim 21 further comprising a suitable adjuvant.

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23. The vaccine composition of claim 22 wherein the adjuvant facilitates breaking of autotolerance to autoantigens.

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24. The vaccine composition of claim 22 wherein the adjuvant is selected from the group consisting of: Adjuvant 65, Freund's complete or incomplete adjuvant, aluminum hydroxide, aluminum phosphate, alum, hexadecylamine, octadecylamine, lysolecithin, dimethyldioctadecylammonium bromide, N,N-dioctadecyl-N',N'-bis(2-hydroxymethyl) propanediamine, methoxyhexadecylglycerol, pluronic polyols; polyanions, pyran, dextran sulfate, poly IC, polyacrylic acid, carbopol; muramyl dipeptide, dimethylglycine tuftsin, oil emulsions and combinations thereof.

25. An antibody or antibody fragment that selectively binds to the canine receptor activator of NF- κ B ligand comprising the amino acid sequence of SEQ ID NO:2.

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26. The antibody of claim 25 that is a monoclonal antibody.

27. A method for inhibiting canine receptor activator of NF- κ B ligand activity in a mammal, comprising administering to the mammal an amount of the antibody or fragment thereof of claim 25 that is effective to inhibit canine receptor activator of NF- κ B ligand activity in the mammal.

10 28. The method of claim 27 wherein the antibody or fragment thereof is administered at a frequency and for a duration sufficient to maintain bone mass or bone density in the mammal at a level equal to or greater than the bone mass or bone density measured prior to the step of administering the antibody or fragment thereof.

15 29. A method for inhibiting receptor activator of NF- κ B ligand activity in a mammal, comprising administering to the mammal an amount of a receptor activator of NF- κ B ligand immunogenic composition of claim 6, that is effective to elicit antibodies that selectively bind to the receptor activator of NF- κ B ligand in the mammal.

20 30. The method of claim 29 wherein the mammal is selected from the group consisting of a canine, an equine, a feline, a bovine, a porcine and a human.

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31. A method for treating conditions in a mammal characterized by excess resorption of bone, comprising immunizing a mammal with an effective amount of the canine receptor activator of NF- κ B ligand immunogenic composition of claim 6.

30 32. A nucleic acid molecule comprising an open reading frame encoding the canine receptor activator of the NF- κ B ligand immunogenic composition of claim 6.

33. The nucleic acid molecule of claim 32 that is RNA or DNA.
34. A replicable nucleic acid vector comprising the nucleic acid molecule of claim 32.
- 5 35. The replicable nucleic vector of claim 34 selected from the group consisting of a plasmid, a phage, a cosmid, a mini-chromosome, and a virus.

36. The replicable nucleic vector of claim 34 that is suitable for expression of the vector by a eukaryotic host cell, a prokaryotic host cell, or both.

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37. The replicable nucleic vector of claim 34, comprising a suitable promotor operably linked 5' to the open reading frame of the canine receptor activator of NF- κ B ligand immunogenic composition.

15 38. The replicable nucleic vector of claim 37 further comprising an operably linked nucleic acid sequence encoding a leader peptide enabling secretion or membrane integration of the canine receptor activator of NF- κ B ligand immunogenic composition.

39. A host cell comprising the replicable nucleic acid vector of claim 34.

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40. The host cell of claim 39 that is a microorganism selected from the group consisting of a bacterium, a yeast, and a protozoan.

25 41. The host cell of claim 39 that is derived from a multicellular organism selected from a fungus, an insect cell, a plant cell, and a mammalian cell.

42. A method of producing a canine receptor activator of NF- κ B ligand comprising culturing the host cell of claim 39 under conditions suitable for expressing the canine receptor activator of NF- κ B ligand.

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43. A method for inhibiting receptor activator of NF- κ B ligand activity in a mammal, comprising administering to the mammal an amount of a nucleic acid vector of claim 34, wherein the nucleic acid vector is suitable for expressing canine receptor activator

of NF- κ B ligand *in vivo* in the mammal, thereby eliciting an immune response effective to inhibit receptor activator of NF- κ B ligand activity in the mammal.

44. A stable cell line comprising the vector of claim 34.

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45. The stable cell line of claim 44 that secretes a canine receptor activator of NF- κ B ligand immunogenic composition or that expresses a canine receptor activator of NF- κ B ligand immunogenic composition on its surface.

10 46. Use of a canine receptor activator of NF- κ B ligand immunogenic composition for the preparation of a vaccine comprising an adjuvant for down-regulating RANKL activity in an mammal.

15 47. Use of a canine receptor activator of NF- κ B ligand for the preparation of a vaccine comprising an adjuvant for the treatment, prophylaxis or amelioration of osteoporosis or other conditions characterized by excessive bone resorption.